

REMARKS


Claims 1-8 and 10-15 are presented. Claims 1, 4-8, 10-12, and 14-15 have been amended. Claim 9 has been canceled and no claims have been added.

The claims have been amended to remove multiple dependencies and to effect minor editorial amendments and are not intended to alter the scope or meaning of the original claims.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "Version with markings to show changes made." Entrance of the foregoing amendments and an early and favorable Action is respectfully requested.

Respectfully submitted,

Date: 6/19/01

  
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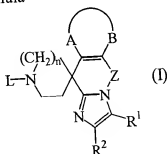
## VERSION WITH MARKINGS TO SHOW CHANGES MADE

## In the Claims:

Please cancel claim 9.

Please amend claims 1, 4-8, 10-12, and 14-15 as follows:

1. (Amended) A compound of formula



or a prodrug, a *N*-oxide, an addition salt, a quaternary amine or a stereochemically isomeric form thereof wherein

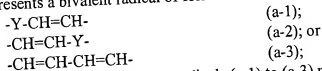
$R^1$  is hydrogen,  $C_{1-6}$ alkyl, halo, formyl, carboxyl,  $C_{1-6}$ alkyloxycarbonyl,  $C_{1-6}$ alkylcarbonyl,  $N(R^3R^4)C(=O)-$ ,  $N(R^3R^4)C(=O)N(R^5)-$ , ethenyl substituted with carboxyl or  $C_{1-6}$ alkyloxycarbonyl, or  $C_{1-6}$ alkyl substituted with hydroxy, carboxyl,  $C_{1-6}$ alkyloxy,  $C_{1-6}$ alkyloxycarbonyl,  $N(R^3R^4)C(=O)-$ ,  $C_{1-6}$ alkyl  $C(=O)N(R^5)-$ ,  $C_{1-6}$ alkyl  $S(=O)_2N(R^5)-$  or  $N(R^3R^4)C(=O)N(R^5)-$ ;

wherein each  $R^3$  and each  $R^4$  independently are hydrogen or  $C_{1-4}$ alkyl;

$R^5$  is hydrogen or hydroxy;

$R^2$  is hydrogen,  $C_{1-6}$ alkyl, hydroxy  $C_{1-6}$ alkyl,  $C_{1-6}$ alkyloxy  $C_{1-6}$ alkyl,  $N(R^3R^4)C(=O)-$ , aryl or halo;  $n$  is 1 or 2;

-A-B- represents a bivalent radical of formula



wherein each hydrogen atom in the radicals (a-1) to (a-3) may independently be replaced by  $R^6$  wherein  $R^6$  is selected from  $C_{1-6}$ alkyl, halo, hydroxy,  $C_{1-6}$ alkyloxy, ethenyl substituted with carboxyl or  $C_{1-6}$ alkyloxycarbonyl, hydroxy  $C_{1-6}$ alkyl, formyl, carboxyl [and] or hydroxycarbonyl  $C_{1-6}$ alkyl;

each  $Y$  independently is a bivalent radical of formula -O-, -S- or -NR<sup>7</sup>-; wherein  $R^7$  is hydrogen,  $C_{1-6}$ alkyl or  $C_{1-6}$ alkylcarbonyl;

$Z$  is [is] a bivalent radical of formula

$-(CH_2)_p-$  (b-1),  
 $-CH=CH-$  (b-2),  
 $-CH_2-CHOH-$  (b-3),  
 $-CH_2-O-$  (b-4),  
 $-CH_2-C(=O)-$  (b-5), or  
 $-CH_2-C(=NOH)-$  (b-6),

[provided] with the proviso that the bivalent radicals (b-3), (b-4), (b-5) and (b-6) are connected to the nitrogen of the imidazole ring via their  $-CH_2-$  moiety;

wherein p is 1, 2, 3 or 4;

L is hydrogen;  $C_{1-6}$ alkyl;  $C_{2-6}$ alkenyl;  $C_{1-6}$ alkylcarbonyl;  $C_{1-6}$ alkyloxycarbonyl;  $C_{1-6}$ alkyl substituted with one or more substituents each independently selected from hydroxy, carboxyl,  $C_{1-6}$ alkyloxy,  $C_{1-6}$ alkyloxycarbonyl, aryl, aryloxy, cyano or  $R^8HN-$  wherein  $R^8$  is hydrogen,  $C_{1-6}$ alkyl,  $C_{1-6}$ alkyloxycarbonyl,  $C_{1-6}$ alkylcarbonyl; or

L represents a radical of formula

$-Alk-Y-Het^1$  (c-1),  
 $-Alk-NH-CO-Het^2$  (c-2) or  
 $-Alk-Het^3$  (c-3); wherein

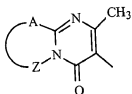
Alk represents  $C_{1-4}$ alkanediyl;

Y represents O, S or NH;

Het<sup>1</sup> [,] and Het<sup>2</sup> [and Het<sup>3</sup>] each represent furanyl, tetrahydrofuranyl, thienyl, oxazolyl, thiazolyl or imidazolyl each optionally substituted with one or two  $C_{1-4}$ alkyl substituents; pyrrolyl or pyrazolyl optionally substituted with formyl, hydroxy,  $C_{1-4}$ alkyl, hydroxycarbonyl,  $C_{1-4}$ alkyloxycarbonyl or with one or two  $C_{1-4}$ alkyl substituents; thiadiazolyl or oxadiazolyl optionally substituted with amino or  $C_{1-4}$ alkyl; pyridinyl, pyrimidinyl, pyrazinyl or pyridazinyl each optionally substituted with  $C_{1-4}$ alkyl,  $C_{1-4}$ alkyloxy, amino, hydroxy or halo; and

Het<sup>3</sup> [may also] represents furanyl, tetrahydrofuranyl, thienyl, oxazolyl, thiazolyl or imidazolyl each optionally substituted with one or two  $C_{1-4}$ alkyl substituents; pyrrolyl or pyrazolyl optionally substituted with formyl, hydroxy,  $C_{1-4}$ alkyl, hydroxycarbonyl,  $C_{1-4}$ alkyloxycarbonyl or with one or two  $C_{1-4}$ alkyl substituents; thiadiazolyl or oxadiazolyl optionally substituted with amino or  $C_{1-4}$ alkyl; pyridinyl, pyrimidinyl, pyrazinyl or pyridazinyl each optionally substituted with  $C_{1-4}$ alkyl,  $C_{1-4}$ alkyloxy, amino, hydroxy, halo, 4,5-dihydro-5-oxo-1H-tetrazolyl substituted

with C<sub>1-4</sub> alkyl, 2-oxo-3-oxazolidinyl, 2,3-dihydro-2-oxo-1H-benzimidazol-1-yl or a radical of formula



wherein

A-Z represents S-CH=CH, S-CH<sub>2</sub>-CH<sub>2</sub>, S-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>, CH=CH-CH=CH, or CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>;

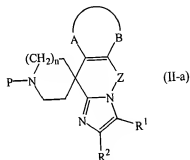
aryl is phenyl or phenyl substituted with 1, 2 or 3 substituents each independently selected from halo, hydroxy, C<sub>1-4</sub> alkyl, polyhaloC<sub>1-4</sub> alkyl, cyano, aminocarbonyl, C<sub>1-4</sub> alkoxy or polyhaloC<sub>1-4</sub> alkoxy;

[provided] with the proviso that 5,6-dihydrospiro[imidazo[1,2-b][3]benzazepine-11[11H],4'-piperidine] and pharmaceutically acceptable addition salts thereof are not included.

4. (Amended) A compound according to [any one of the preceding] claim[s] 1 wherein -A-B- is a bivalent radical of formula -CH=CH-CH=CH- (a-3) or -CH=CH-Y- (a-2).
5. (Amended) A compound according to [any one of the preceding] claim[s] 1 wherein Z is - (CH<sub>2</sub>)<sub>p</sub>- (b-1), -CH=CH- (b-2), or -CH<sub>2</sub>-O- (b-4).
6. (Amended) A compound according to claim[s] 1, [2, 4 or 5] wherein L is hydrogen, C<sub>1-6</sub> alkyl, hydroxyC<sub>1-6</sub> alkyl, carboxyC<sub>1-6</sub> alkyl, C<sub>1-6</sub> alkoxy carbonyl, or C<sub>1-6</sub> alkoxy carbonylC<sub>1-6</sub> alkyl.
7. (Amended) A compound according to [any one of the preceding] claim[s] 1 wherein R<sup>1</sup> is hydroxyC<sub>1-6</sub> alkyl, formyl, C<sub>1-6</sub> alkoxy carbonyl, C<sub>1-6</sub> alkoxyC<sub>1-6</sub> alkyl, N(R<sup>3</sup>R<sup>4</sup>)C(=O)-, halo or hydrogen.
8. (Amended) A compound according to claim 1 wherein the compound is 5,6-dihydrospiro[11H-imidazo[2,1-b][3]benzazepine-11,4'-piperidine]-3-carboxamide dihydrochloride; 1'-butyl-5,6-dihydrospiro[imidazo[2,1-b][3]benzazepine-11[11H],4'-piperidine]; 6,11-dihydro-1'-methylspiro[5H-imidazo[2,1-b][3]benzazepine-11,4'-piperidine] cyclohexylsulfamate(1:2);

6,11-dihydrospiro[5-imidazo[2,1-b][3]benzazepine-11,4'-piperidine]-3-methanol] (E)-2-butenedioate (2:1);  
 3-chloro-6,11-dihydrospiro[5H-imidazo[2,1-b][3]benzazepine-11,4'-piperidine] (E)-2-butenedioate (1:1);  
 6,11-dihydro-3-(methoxymethyl)spiro[5H-imidazo[2,1-b][3]benzazepine-11,4'-piperidine] (E)-2-butenedioate (1:1);  
 6,11-dihydro-1'-(2-hydroxyethyl)spiro[5H-imidazo[2,1-b][3]benzazepine-11,4'-piperidine]-3-carboxamide;  
 6,11-dihydro-1'-methylspiro[5H-imidazo[2,1-b][3]benzazepine-11,4'-piperidine]-3-carboxamide monohydrate;  
 ethyl 3-(aminocarbonyl)-6,11-dihydro- $\alpha$ -phenylspiro[5H-imidazo[2,1-b][3]benzazepine-11,4'-piperidine]-1'-propanoate monohydrochloride;  
 3-(aminocarbonyl)-6,11-dihydrospiro[5H-imidazo[2,1-b][3]benzazepine-11,4'-piperidine]-1'-carboxylate;  
 spiro[10H-imidazo[1,2-a]thieno[3,2-d]azepine-10,4'-piperidine];  
 6,11-dihydrospiro[5H-imidazo[2,1-b][3]benzazepine-11,4'-piperidine]-2,3-dicarboxamide dihydrochloride monohydrate; or  
 a prodrug, a N-oxide, an addition salt, a quaternary amine or a stereochemically isomeric form thereof.

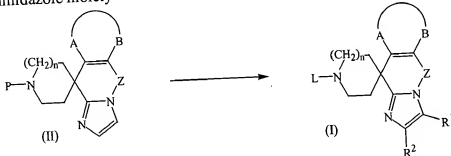
10. (Amended) A pharmaceutical composition comprising a pharmaceutically acceptable carrier, and as active ingredient a therapeutically effective amount of a compound as [described] defined in [any one of] claim[s] 1 [to 9].
11. (Amended) A process of preparing a composition as claimed in claim 10, [characterized in that,] wherein a pharmaceutically acceptable carrier is [intimately] mixed with a therapeutically effective amount of a compound as [described] defined in [any one] claim[s] 1 [to 9].
12. (Amended) A compound of formula



or a *N*-oxide, an addition salt, a quaternary amine or a stereochemically isomeric form thereof wherein P is a protective group and n, -A-B-, Z, R<sup>1</sup> and R<sup>2</sup> are defined as in claim 1, [provided] with the proviso that 6,11-dihydro-1'-(phenylmethyl)-5*H*-spiro[imidazo[1,2-b][3]benzazepine-11,4'-piperidine] (E)-2-butenedioate(1:2) is not included.

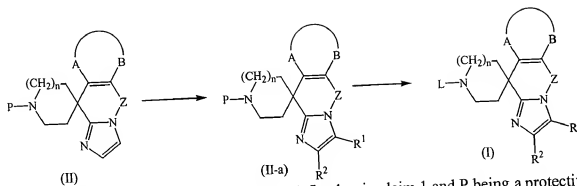
14. (Amended) A process of preparing a compound as claimed in claim 1, [characterized by,] comprising

- a) deprotecting an intermediate of formula (II), followed optionally by derivatizing either the piperidine moiety, or the imidazole moiety, or both the piperidine moiety and the imidazole moiety



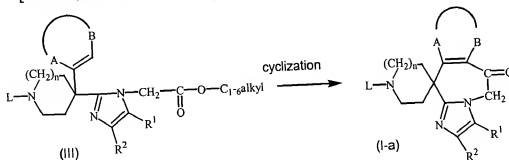
with [-A-B-, Z, L, R<sup>1</sup> and R<sup>2</sup>, and n defined as in claim 1 and] P being a protective group;

- b) derivatizing an intermediate of formula (II) at the imidazole moiety, [leading to the formation of] to form an intermediate of formula (II-a), followed by deprotecting the piperidine moiety, and followed optionally by derivatizing the piperidine moiety



[with -A-B-, Z, L, R<sup>1</sup> and R<sup>2</sup>, and n defined as in claim 1 and P being a protective group;]

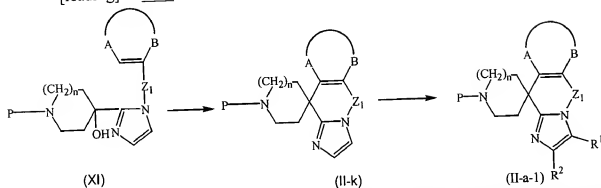
- c) [by] cyclizing an intermediate of formula (III) in the presence of an appropriate acid,  
[resulting in] to form a compound of formula (I-a)



[with -A-B-, L, R<sup>1</sup> and R<sup>2</sup>, and n defined as in claim 1;]  
and, [if desired] optionally, converting compounds of formula (I) and (I-a) into each other  
[following art-known transformations], and further, [if desired] optionally, converting the  
compounds of formula (I), into a therapeutically active non-toxic acid addition salt by  
treatment with an acid, or into a therapeutically active non-toxic base addition salt by  
treatment with a base, or [conversely,] converting the acid addition salt form into the free  
base by treatment with alkali, or converting the base addition salt into the free acid by  
treatment with acid; and, [if desired] optionally, preparing stereochemically isomeric forms  
or N-oxide forms thereof.

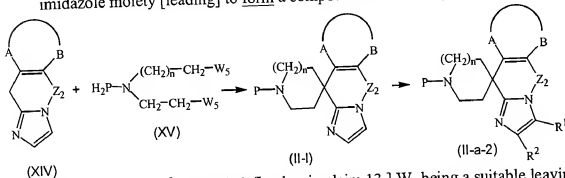
15. (Amended) A process of preparing a compound as claimed in claim [12] 13, [characterized  
by] comprising,  
a) cyclizing a compound of formula (XI) with an appropriate acid, [leading] to form a  
compound of formula (II-k), followed optionally by derivatizing the imidazole moiety,

[leading] to form a compound of formula (II-a-1)



with [-A-B-, R<sup>1</sup>, R<sup>2</sup>, n and P defined as in claim 13, and] Z<sub>1</sub> being a bivalent radical of formula -(CH<sub>2</sub>)<sub>p</sub>-, wherein p is 1,2,3 or 4[ ] ; and

- b) [by] reacting a tricyclic moiety of formula (XIV) with a reagent of formula (XV) under an inert atmosphere in a reaction inert solvent in the presence of a suitable base, [leading the] to form a compound of formula (II-l), followed optionally by derivatizing the imidazole moiety [leading] to form a compound of formula (II-a-2)



with [-A-B-, R<sup>1</sup>, R<sup>2</sup>, n and P defined as in claim 13,] W<sub>5</sub> being a suitable leaving group, [e.g. a halo,] and Z<sub>2</sub> being a bivalent radical of formula -(CH<sub>2</sub>)<sub>p</sub>-, or -CH<sub>2</sub>-O-, wherein p is 1,2,3 or 4.